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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/694,245	10/27/2003	Timothy A. Morris	1133.005US2	4050

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EXAMINER	
GRUN, JAMES LESLIE	
ART UNIT	PAPER NUMBER
1641	
MAIL DATE	DELIVERY MODE
09/24/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/694,245	MORRIS, TIMOTHY A.	
	Examiner	Art Unit	
	James L. Grun	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *23 July 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-32,35-40 and 49-52* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-32,35-40 and 49-52* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

The amendment filed 23 July 2007 is acknowledged and has been entered. Claims 49-52 are newly added. Claims 33, 34, and 41-48 have been cancelled. Claims 1-32, 35-40 and 49-52 remain in the case.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention, and failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure.

The specification is objected to and claims 1-32, 35-40 and 49-52 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons similar to those of record in the prior rejection of the similar subject matter of prior claims 1-37 as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The specification, as originally filed, does not provide written description support for an antibody, antiserum, or other detection reagent having a ratio of IC_{50} for fibrinogen to that of des-arginine fibrinopeptide B or fibrinopeptide B of at least 0.34, or about 0.5, as is now

claimed. The specification, as originally filed, also does not provide written description support for an antibody, antiserum, or other detection reagent having a ratio of IC_{50} for des-arginine fibrinopeptide B to that of fibrinopeptide B of about 0.75 as is now claimed. The specification, as originally filed, does not provide written description support for an antibody, antiserum, or other detection reagent that binds to des-arginine fibrinopeptide B and/or fibrinopeptide B and does not cross-react with fibrinogen with an IC_{50} ratio of at least 0.34 as is now claimed. Applicant discloses that a single polyclonal antiserum comprising a single bleeding of a single rabbit (i.e. R4097, bleed I3) elicited by immunization with human fibrinopeptide B was selected as having the "best reactivity profile" for use and that this antiserum as a whole: had a cross-reactivity with des-arginine fibrinopeptide B which was 75% of that with fibrinopeptide B as determined by IC_{50} values in a competitive enzyme-linked immunosorbent assay in which the competitive inhibition of the binding of the antibody to human fibrinopeptide B by the peptides was determined and related in a particular fashion (i.e. the IC_{50} for fibrinopeptide B divided by the IC_{50} for des-arginine fibrinopeptide B was 0.75); reacted with fibrinogen better than with fibrinopeptide B (i.e. the IC_{50} for fibrinogen (2.3 nM) divided by the IC_{50} for fibrinopeptide B (6.7 nM) was 0.34) (see e.g. pages 27-28 and 40-41). The instantly claimed invention also does not set forth the relevant comparison for determining the difference in IC_{50} values. Although one of skill in the art might realize from reading the disclosure that antibodies binding with cross-reactivities as are now claimed are useable in the invention, such possibility of use does not provide explicit or implicit indication to one of skill in the art that an antibody with such cross-reactivity ranges as are now claimed was originally contemplated as part of applicant's invention, particularly since applicant does not disclose such a reactivity profile for the antibody and

exemplifies a single polyclonal antibody which meets only specific limits of the ranges as are now claimed, and such possibility of use does not satisfy the written description requirements of 35 U.S.C. § 112, first paragraph. Note that a description which renders obvious a claimed invention is not sufficient to satisfy the written description requirement. Applicant is requested to direct the Examiner's attention to specific passages where support for these newly recited limitations can be found in the specification as filed or is required to delete the new matter.

The examiner would note that applicant also does not provide adequate written description of a single isolated antibody or fragment thereof having the properties of the exemplified polyclonal antibody population as are now claimed. Adequate written description requires more than a mere statement that a product is part of the invention and a reference to a potential method of isolating it. The product itself is required. Furthermore, in *The Reagents of the University of California v. Eli Lilly* (43 USPQ2d 1398-1412), the court held that a generic statement which defines a genus of products by only their functional activity does not provide an adequate written description of the genus.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115). However, the reproducibility of an antiserum with properties as claimed would seem unknown and unpredictable in view of the disclosure that only a single bleeding from a single immunized rabbit, selected as best for use, had properties close to those as claimed. Absent further written description and guidance, one would have no assurance of predictably obtaining additional polyclonal antibody populations with the relevant properties for use. The variability of

polyclonal antisera binding properties after immunization with fibrinopeptide B is clearly shown in Wilner et al. (Biochem. 18: 5078, 1979).

In view of the lack of adequate written description of a single isolated antibody or fragment thereof having even the properties of the polyclonal antibody population noted above, one would therefore also have no assurance of the predictable ability to obtain and use an isolated or monoclonal antibody, or fragment thereof, with the properties as are now claimed. Moreover, in view of the guidance in the instant specification to no functional isolated species, the amount of experimentation required to determine functional structures, modifications, or properties for any usable species would be undue. Again, note that even an enabling disclosure for the preparation and use of only a few analogs of a product does not enable all possible analogs where the characteristics of the analogs are unpredictable. See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.* (18 USPQ 2d 1027 (CAFC 1991)).

A patent is granted for a completed invention, not the general suggestion of an idea and how that idea might be developed into the claimed invention. In the decision of *Genentech Inc. v. Novo Nordisk*, 42 USPQ 2d 1001 (CAFC 1997), the court held that: "[p]atent protection is granted in return for an enabling disclosure of an invention, not for vague intimations of general ideas that may or may not be workable" and that "[t]ossing out the mere germ of an idea does not constitute enabling disclosure." The court further stated that: "when there is no disclosure of any specific starting material or of any of the conditions under which a process is to be carried out, undue experimentation is required; there is a failure to meet the enablement requirements that cannot be rectified by asserting that all the disclosure related to the process is within the skill

of the art", "[i]t is the specification, not the knowledge of one skilled in the art, that must supply the novel aspects of an invention in order to constitute adequate enablement."

Claims 7, 9-10, 27, 31, 36, and 39 are rejected under 35 U.S.C. 112, first paragraph, for the reasons of record as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention, and which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. The specification does not reasonably provide description of or enablement for any cell line producing a monoclonal antibody as instantly claimed.

Applicant's arguments filed 23 July 2007 have been fully considered but they are not deemed to be persuasive.

Notwithstanding applicant's assertions to the contrary, applicant's amendments have not obviated rejections under this statute for the reasons set forth above.

Applicant urges that the specification describes the invention as claimed. This is not found persuasive for the reasons of record and as set forth above.

Applicant urges that disclosure of methods to make antibodies adequately describe and enable the invention as claimed. These are not found persuasive because, as set forth, adequate written description requires more than a mere statement that a product is part of the invention, more than a reference to a potential method of isolating it, and more than a generic statement

which defines a genus of products by only their functional activity. As set forth, the product itself is required as well as recitation of a representative number of products falling within the scope of a claimed genus. Moreover, as set forth, all possible analogs of a product are not enabled by a disclosure wherein the characteristics of the analogs are unpredictable. Notwithstanding applicant's assertions to the contrary, the relevant structure of any complementarity determining regions of antibody variable chains which bind to the antigen are not known, and, as set forth previously, the state of the art is such that one cannot readily envision structures, including antibody structures, which bind or do not bind the antigen. Thus, one cannot correlate functional characteristics with a known or disclosed structure because no particular structure for a particular antibody that binds to the antigen with the relevant binding properties has been disclosed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-32, 35-40 and 49-52 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In claim 1 and claims dependent thereupon, "the ratio" lacks antecedent basis. It is believed --thereof-- was intended at line 6.

In claim 11 and claims dependent thereupon, the method is not clear because it is not clear how complex is present in the sample or how detection of the presence of complex relates to later claimed peptide concentrations.

In claim 29 and claims dependent thereupon, recitations of "the amount" lack antecedent basis.

In claim 52, "the ratio" lacks antecedent basis.

Applicant's arguments filed 23 July 2007 have been fully considered but they are not deemed to be persuasive. Notwithstanding applicant's assertions to the contrary, applicant's amendments have not obviated rejections under this statute for the reasons set forth above.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(e) the invention was described in-
(1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or
(2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent,
except that an international application filed under the treaty defined in section 351(a) shall have the effects for the purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language;

Claims 1-7, 9-15, 21-27, 35, 36, 49, 51, and 52 are rejected under 35 U.S.C. § 102(e)(2) as being clearly anticipated by Kudryk et al. (US 5,876,947) for reasons of record in the prior rejection of the similar subject matter of claims 1-7, 9-15, 21-27, 35, and 36.

Claims 38 and 39 are rejected under 35 U.S.C. § 102(e)(2) as being anticipated by Kudryk et al. (US 5,876,947) for reasons of record.

Claims 1-7, 9-15, 21-27, 35, 36, 49, 51, and 52 are rejected under 35 U.S.C. § 102(a) as being clearly anticipated by Kudryk et al. (WO 99/05176) for reasons of record in the prior rejection of the similar subject matter of claims 1-7, 9-15, 21-27, 35, and 36.

Claims 38 and 39 are rejected under 35 U.S.C. § 102(a) as being anticipated by Kudryk et al. (WO 99/05176) for reasons of record.

Applicant's arguments filed 23 July 2007 have been fully considered but they are not deemed to be persuasive.

Applicant urges that the P10 monoclonal antibody, as specifically exemplified in the references of Kudryk et al., does not have the binding reactivity with fibrinogen as is now claimed. This is not found persuasive because the disclosure of the reference is considered as a whole and is not limited to that which is specifically exemplified. As set forth, Kudryk et al. disclose monospecific antibodies which bind to an epitope as present in fibrinogen, fibrinopeptide B, or des-Arg fibrinopeptide B (SEQ ID NO:1) without regard to whether the epitope is in native protein or whether the C-terminal Arg residue has been cleaved from the fibrinopeptide B or whether the N-terminal residue is glutamine or pyroglutamic acid. As fibrinogen contains 2 moles of fibrinopeptide B (see e.g. col. 21 in US '947), such an ideal antibody of the invention would inherently have the IC_{50} ratios as instantly claimed.

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

> (c) Subject matter developed by another person, which qualifies as prior art only under one or more subsections (e), (f) and (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

Claims 38 and 40 are rejected under 35 U.S.C. § 102(b) as being anticipated by, or under 35 U.S.C. § 103 (a) as being unpatentable over, Qureshi et al. (Thromb. Haemostasis 42:1316, 1979) in light of Eckhardt et al. (J. Clin. Invest. 67:809, 1981), Bilezikian et al. (J. Clin. Invest. 56:438, 1975), and Wilner et al. (Biochemistry 18:5078, 1979) for reasons similar to those of record. The examiner cannot determine from the disclosures of the references the cross-reactivity of the antiserum taught thereby with fibrinogen. Inherently or implicitly, the antibody has the properties as instantly claimed. The Patent and Trademark Office does not have the facilities and resources to provide the *factual* evidence needed in order to establish that there is a difference, in the first place, between the reagents of the prior art and those instantly disclosed and, that if there is such a difference, that such a difference would have been considered unexpected, i.e. unobvious, by one of ordinary skill in the art. The burden is upon applicant to present such factual evidence. See e.g. In re Best (195 USPQ 430 (CCPA 1977)) or Ex parte Phillips (28 USPQ2d 1302 (BPAI 1993)).

Applicant's arguments filed 23 July 2007 have been fully considered but they are not deemed to be persuasive. Applicant's arguments drawn to the use of the reagents in a method were not found persuasive because the arguments were not germane to the components of the kit as claimed.

Claims 1-17, 21-32, 35-40, 49, 51 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kudryk et al. (US 5,876,947), in view of Eckhardt et al. (J. Clin. Invest. 67:809, 1981) for reasons of record in the prior rejection of the similar subject matter of claims 1-17, 21-32, and 35-40.

Claims 1-17, 21-32, 35-40, 49, 51 and 52 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kudryk et al. (WO 99/05176), in view of Eckhardt et al. (J. Clin. Invest. 67:809, 1981) for reasons of record in the prior rejection of the similar subject matter of claims 1-17, 21-32, and 35-40.

Applicant's arguments filed 23 July 2007 have been fully considered but they are not deemed to be persuasive. Applicant's arguments regarding the references of Kudryk et al. (US 5,876,947 or WO 99/05176) have been addressed previously in this Office action and the examiner's arguments thereto are incorporated herein.

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 38-40 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-23 of U.S. Patent No. 6,673,561, if necessary, in view of Kudryk et al. (US 5,876,947 or WO 99/05176) for the reasons of record.

Claims 1-14, 18-32, 35-37, 49, 51, and 52 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-23 of U.S. Patent No. 6,673,561, in view of Kudryk et al. (US 5,876,947 or WO 99/05176) for reasons of record and as set forth above.

Applicant's arguments filed 23 July 2007 have been fully considered but they are not deemed to be persuasive. Applicant's arguments regarding the references of Kudryk et al. (US 5,876,947 or WO 99/05176) have been addressed previously in this Office action and the examiner's arguments thereto are incorporated herein.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR REPLY TO THIS FINAL ACTION IS SET TO EXPIRE **THREE MONTHS** FROM THE MAILING DATE OF THIS ACTION. IN THE EVENT A FIRST REPLY IS FILED WITHIN **TWO MONTHS** OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE **THREE-MONTH** SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR REPLY EXPIRE LATER THAN **SIX MONTHS** FROM THE MAILING DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to James L. Grun, Ph.D., whose telephone number is (571) 272-0821. The examiner can normally be reached on weekdays from 9 a.m. to 5 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le, SPE, can be contacted at (571) 272-0823.

The phone number for official facsimile transmitted communications to TC 1600, Group 1640, is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application, or requests to supply missing elements from Office communications, should be directed to the Group receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/JLG/
James L. Grun, Ph.D.
September 15, 2007

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